REMARKS

Claims 1, 21-25, 35, and 59 have been amended to more clearly describe the invention. Support for the amendments can be found in the specification at, for example, page 14, lines 24-27, page 18 lines 11-18, and page 19, lines 20-23. Claim 26 has been canceled. New claims 61-66 have been added. No new matter has been introduced. Claims 1-25, 27-56, and 59-66 are pending.

Rejections withdrawn

Applicants thank the Examiner for withdrawing previous rejections under 35 U.S.C. § 112, second paragraph, and under 35 U.S.C. § 102(b) with respect to WO 98/04740 by Mirkin et al.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1-56, 59 and 60 under 35 U.S.C. § 112, first paragraph, for lack of enablement. See pages 7-12 of the Office Action.

The Examiner has indicated that the specification is enabling for "a semiconductor nanocrystal, a linking group which binds to the outer surface of the nanocrystal and has an ionizable moiety, and a protein having an ionizable moiety, wherein the nanocrystal and the protein are linked by an identified linking group to form an ionic conjugate." See the Office Action at page 7. The Examiner contends that the specification does not enable

> a composition comprising an inorganic particle, a linking group which binds to the outer surface of the inorganic particle and has an ionizable moiety, an a macromolecule having an ionizable moiety, wherein the inorganic particle and the macromolecule are linked by a linking group to form an ionic conjugate, and a method of forming the ionic conjugate, where the inorganic particle, the linking group, and the macromolecule are not defined.

See the Office Action at page 7.

Applicants have discovered a composition and a method of making an ionic conjugate that includes an inorganic particle (or semiconductor nanocrystal) and a linking group which has a distal end and a proximal end. The distal end is bound to an outer surface of the inorganic

particle (or semiconductor nanocrystal) and the proximal end includes a first charged or ionizable moiety. The distal end includes S, N, P, O, or O=P, the proximal end includes a hydroxide, an alkoxide, a carboxylate, a sulfonate, a phosphate, a phosphonate, or a quaternary ammonium, and the distal and proximal ends are connected by a spacer. The composition can also include a macromolecule having a second charged or ionizable moiety, the second charged or ionizable moiety having a plurality of charged or ionizable groups. Alternatively, the composition can include a fusion protein including a second charged or ionizable moiety. The first and second charged or ionizable moieties electrostatically associate the semiconductor nanocrystal with the macromolecule or fusion protein to form an ionic conjugate. See independent claims 1 and 21.

Applicants have also discovered a method of forming an ionic conjugate that includes providing an inorganic particle (or semiconductor nanocrystal) including a linking group having a distal end and a proximal end, the distal end being bound to an outer surface of the inorganic particle (or semiconductor nanocrystal). The distal end is bound to an outer surface of the semiconductor nanocrystal and the proximal end includes a first charged or ionizable moiety. The distal end includes S, N, P, O, or O=P, the proximal end includes a hydroxide, an alkoxide, a carboxylate, a sulfonate, a phosphate, a phosphonate, or a quaternary ammonium, and the distal and proximal ends are connected by a spacer. The method also includes contacting a macromolecule or fusion protein having a second charged or ionizable moiety, the second charged or ionizable moiety having a plurality of charged or ionizable groups, with the inorganic particle or semiconductor nanocrystal. The first and second charged or ionizable moieties electrostatically associate the inorganic particle or semiconductor nanocrystal with the macromolecule or fusion protein to form an ionic conjugate. See independent claims 35 and 59.

Inorganic particles are described in the specification at, for example, pages 9-10. In particular, the specification indicates that inorganic colloids include Ag, Au, or a phosphor (page 9, lines 27-30). Inorganic colloids including Au are described, for example, in WO 98/04740 to Mirkin et al. This is but one example of inorganic particles known in the art. A person skilled in the art, upon reading the specification and using the knowledge in the art, would be able to make and use the inorganic particles.

The Examiner has indicated that the claims are enabled if limited to an "identified linking group" (see page 7 of the Office Action). The independent claims have been amended to describe the linking group as having a distal end being bound to an outer surface of the

semiconductor nanocrystal and including S, N, P, O, or O=P. The linking group also has a proximal end including a first charged or ionizable moiety and including a hydroxide, an alkoxide, a carboxylate, a sulfonate, a phosphate, a phosphonate, or a quaternary ammonium. The distal and proximal ends are connected by a spacer. See the specification, for example, at page 17, line 20 - page 18, line 3, and page 18, lines 11-17, describing the linking groups. The linking group is an identified linking group.

According to the American Heritage Dictionary of the English Language, Fourth Edition, (as provided at dictionary.reference.com), the word "macromolecule" is defined as "a very large molecule, such as a polymer or protein, consisting of many smaller structural units linked together." A person of ordinary skill in the art would recognize that organic polymers, nucleic acids, and polypeptides are all examples of macromolecules. The specification provides further description of ionic conjugates that include a non-protein macromolecule can be found at page 17, lines 9-19.

At page 14, the specification states "[t]he macromolecule can include a plurality of ionizable groups such [as] in polylysine, poly (acrylic acid) (PAA), poly (allyl amine hydrochloride) (PAH), sulfonated polystyrene (SPS), and polydiallyldimethylammonium chloride (PDADMAC)." Claims 1 and 35 refer to the macromolecule including a second charged or ionizable moiety having a plurality of charged or ionizable groups. Additional support for the macromolecule including a plurality of ionizable groups can be found in Figs. 3A and 4A. The macromolecule is a defined macromolecule.

The claims are enabled. In particular, Applicants believe that independent claims 21 and 59, and the claims that depend from them, are directed to subject matter that the Examiner has specifically indicated is enabled (see page 7 of the Office Action). Similarly, Applicants believe that claims 61 and 64 are directed to subject matter that the Examiner has specifically indicated is enabled. Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Obviousness-type Double Patenting Rejections

The '610 Patent

Claims 1-9, 11-13, 15, 16, 35-43, 45-47, 49 and 50 have been rejected by the Examiner under the judicially created doctrine of obviousness-type double patenting over claims 1-10, 16-

18, 29-32, 37, 38 and 45-57 of U.S. Patent No. 6,306,610 ("the '610 patent"). See pages 3-5 of the Office Action. Claims 2-9, 11-13, 15, and 16 depend from claim 1, and claims 36-43, 45-47, 49 and 50 depend from claim 35.

The Examiner contends that claims 1-10, 16-18, 29-32, 37, 38 and 45-57 of the '610 patent disclose

> A composition comprising a first member of a binding pair; a semiconductor nanocrystal core linked to the first member, and an outer layer including a ligand comprising a multidentate molecule or a molecule having formula of $H_zX((CH_2)CO_2H)_y$, where the link between the first member of a binding pair and the nanocrystal compris[es] a linking group for attachment to the nanocrystal and a second portion comprising **a hydrophilic group... which links to the first member by hydrophilic or electrostatic interaction,** and the first member can be a protein (emphasis added).

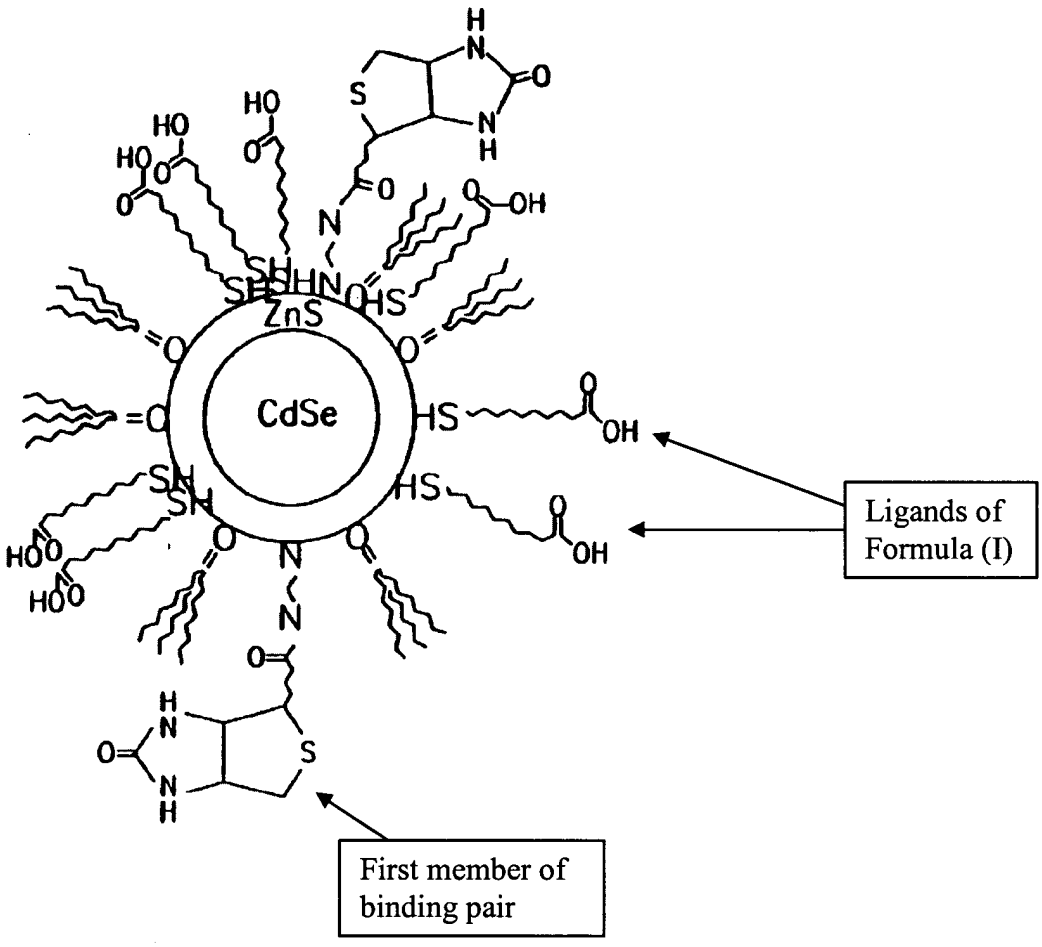
See the Office Action at pages 3-4. Applicants respectfully disagree. Nothing in claims 1-10, 16-18, 29-32, 37, 38 and 45-57 of the '610 patent indicates that "the link between the first member of a binding pair and the nanocrystal compris[es] a linking group for attachment to the nanocrystal and a second portion comprising a hydrophilic group... which links to the first member by hydrophilic or electrostatic interaction."

Claim 1 of the '610 patent recites:

> A composition comprising:
> a first member of a binding pair;
> a semiconductor nanocrystal core linked to the first member, and
> an outer layer including a ligand comprising a multidentate molecule or a molecule having structural formula (I),
>
> $$H_zX((CH_2)_nCO_2H)_y \qquad (I)$$
>
> or a salt thereof, wherein:
> X is the first portion of the ligand and is N, P, or O=P;
> n is greater than or equal to 6; and
> z and y are selected to satisfy the valence requirements of X.

The link is between the first member of the binding pair and the semiconductor nanocrystal. The ligand, which comprises a multidentate molecule or a molecule having formula of $H_zX((CH_2)CO_2H)_y$, is a distinct element of the composition, and not part of the link between the first member of the binding pair and the semiconductor nanocrystal. See, for example,

Figures 8, 9, and 10 of the '610 patent, showing a semiconductor nanocrystal having an outer layer including ligands of formula (I), and, separately and distinctly from the ligands, members of a binding pair (e.g. biotin) linked to the semiconductor nanocrystal. A detail of Figure 9 of the '610 patent is shown below. As illustrated by the Figure, the ligands of the outer layer are distinct from the first member of the binding pair.



Detail of Fig. 9 from the '610 patent

Claim 3 of the '610 patent indicates that the link between the first member of the binding pair and the nanocrystal is an interaction selected from the group consisting of covalent, noncovalent, hydrophobic, hydrophilic, electrostatic, magnetic or coordination through a metal complex. However, there is no teaching or suggestion that the link that can be an electrostatic interaction involves a linking group of any kind. The ligand does not act as a linking group for

linking the first member of the binding pair to the nanocrystal. Nothing in claims 1 or 3 teaches or suggests, as alleged by the Examiner, that the link between the first member of the binding pair and the nanocrystal comprises a "a linking group... comprising a hydrophilic group... which links to the first member by hydrophilic or electrostatic interaction." Claim 3 does not teach or suggest a linking group which has a distal end and a proximal end, the distal end being bound to an outer surface of a semiconductor nanocrystal, and the proximal end including a first charged or ionizable moiety that electrostatically associates with a second charged or ionizable moiety belonging to a macromolecule.

Claim 4 of the '610 patent describes the ligand including a first portion comprising at least one linking group for attachment (of the ligand) to the nanocrystal and a second portion comprising at least one hydrophilic group. Claim 5 of the '610 patent recites "[t]he composition of claim 4, wherein the first member of the binding pair is linked to the second portion of the ligand." While claim 4 indicates that the second portion of the ligand comprises at least one hydrophilic group, claim 5 does not teach or suggest, as the Examiner alleges, a hydrophilic group which links to the first member by hydrophilic or electrostatic interaction. Claim 5 indicates only that the second portion of the ligand is linked to the first member of the binding pair. There is no indication that the link between the second portion of the ligand and the first member of the binding pair involves electrostatic association. These claims do not teach or suggest that the ligand is a linking group which has a distal end and a proximal end, the distal end being bound to an outer surface of a semiconductor nanocrystal, and the proximal end including a first charged or ionizable moiety that electrostatically associates with a second charged or ionizable moiety belonging to a macromolecule.

Furthermore, there is no teaching or suggestion in the claims of the '610 patent of a macromolecule having a charged or ionizable moiety having a plurality of charged or ionizable groups. Nor does the '610 patent provide any teaching, suggestion, or motivation to use a generic inorganic particle in place of a semiconductor nanocrystal.

Indeed, none of the claims of the '610 patent, whether alone or in combination, teach, suggest, or motivate a person skilled in the art to make a linking group which has a distal end and a proximal end, the distal end being bound to an outer surface of a semiconductor nanocrystal and the proximal end including a first charged or ionizable moiety that electrostatically associates with a second charged or ionizable moiety belonging to a macromolecule.

Independent claims 1 and 35, and the claims that depend from them are non-obvious over the claims of the '610 patent. Applicants respectfully request reconsideration and withdrawal of this rejection.

The '144 Patent

Claims 1-5, 8, 9, 11-12, 15, 16, 35-39, 42, 43, 45-46, 49 and 50 have been rejected by the Examiner under the judicially created doctrine of obviousness-type double patenting over claims 1-72 of U.S. Patent No. 6,326,144 ("the '144 patent"). See pages 5-7 of the Office Action. Claims 2-5, 8, 9, 11-12, 15, and 16 depend from claim 1, and claims 36-39, 42, 43, 45-46, 49 and 50 depend from claim 35.

The Examiner contends that the claims of the '144 patent disclose

> A composition comprising a compound; a semiconductor nanocrystal linked to the compound by a ligand of the formula of $H_zX((CH_2)CO_2H)_y$, wherein the compound can be a protein, a peptide or a nucleic acid, and wherein the link between the compound and the nanocrystal is through hydrophilic or electrostatic association.

See the Office Action at page 6.

Applicants have discovered a composition and method of forming an ionic conjugate that includes an inorganic particle, and a linking group which has a distal end and a proximal end. The distal end is bound to an outer surface of the inorganic particle and the proximal end includes a first charged or ionizable moiety. The composition also includes a macromolecule having a second charged or ionizable moiety having a plurality of charged or ionizable groups. The first and second charged or ionizable moieties electrostatically associate the inorganic particle with the macromolecule. See independent claims 1 and 35.

The claims of the '144 patent do not teach, suggest, or motivate a person skilled in the art to make a macromolecule having a second charged or ionizable moiety, where the second charged or ionizable moiety includes a plurality of charged or ionizable groups. The claims of the '144 patent refer to a compound without further description (see claim 1). The compound can be a biological compound, such as "a protein, a peptide, a nucleic acid, a carbohydrate, a cell, a lipid, a cellular organelle, or a signaling molecule" (see, for example, claim 11). Nothing in the claims of the '144 patent teaches or suggests that the compound or any of the biological compounds listed includes a charged or ionizable moiety that includes a plurality of charged or

ionizable groups. Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejections under 35 U.S.C. § 102(e)

Claims 1-9, 11-13, 15, 16, 35-43, 45-47, 49 and 50 have been rejected under 35 U.S.C. § 102(e) as being anticipated by the '610 patent. See pages 12-13 of the Office Action. In addition, claims 1-5, 8, 9, 11-12, 15, 16, 35-39, 42, 43, 45-46, 49 and 50 have been rejected under 35 U.S.C. § 102(e) as being anticipated by the '144 patent. See pages 13-14 of the Office Action.

Applicants of the present claimed invention are George P. Anderson, Hedi Mattoussi, J. Matthew Mauro, Moungi G. Bawendi, and Vikram C. Sundar. It is well established that "one's own work is not prior art under §102(a) even though it has been disclosed to the public in a manner or form which would otherwise fall under 102(a)." *In re Katz*, 215 USPQ 14, 17 (CCPA 1982). The inventors of the '610 and '144 patents are Moungi G. Bawendi, Frederic V. Mikulec and Vikram C. Sundar. The '610 and '144 patents describe a portion of the Applicants' own work and, therefore, are not citable against this application.

The actual contributions of the three co-authors of the '610 and '144 patents (Moungi G. Bawendi, Frederic V. Mikulec and Vikram C. Sundar,) and Applicants are clarified in a Declaration 37 C.F.R. § 1.132 of Moungi G. Bawendi submitted herewith ("the Bawendi declaration," attached at Tab A). Dr. Bawendi states "Mikulec was not involved with any discovery or development of the concepts with regard to a composition including an inorganic particle electrostatically associated with a macromolecule." See paragraph three of the Bawendi declaration. Any disclosure in the '610 patent or the '144 patent relevant to the instantly claimed ionic conjugates is the work of the three co-inventors named in present application. Thus, the neither the '610 patent nor the '144 patent qualifies as prior art under 35 U.S.C. § 102(e). Applicants, therefore, respectfully request that the Examiner reconsider and withdraw this rejection.

New claims

New claims 61-66 have been added. Claims 61-63 depend from claim 1, and claim 64-66 depend from claim 35. Support for the new claims can be found, for example, at page 14, lines

19 and 24-27, and at page 19, lines 20-24 of the specification. No new matter has been added. The new claims are patentable over the cited references.

CONCLUSION

Applicants ask that all claims be allowed. Enclosed is a check for $90 for excess claims fees. Please apply any other charges or credits to deposit account 19-4293.

Respectfully submitted,

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